REMARKS

Rejection of Claims and Traversal Thereof

In the October 28, 2010 Final Office Action:

claims 1-2, 6, 9, 15-16, 26-28. 37 and 81 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita and Figdor, et al. (US Patent No. 7,148,329, hereinafter Figdor);

claims 10 and 52 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita and Figdor and in further view of LaGrone (US Patent No. 5,981,493, hereinafter LaGrone);

claims 58-59 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita, Figdor, LaGrone and in further view of Haas, et al (US Patent Publication No 2005/0181038, hereinafter Hass);

claims 50 and 53 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita, Figdor, LaGrone, Haas and in further view of Charan, et al. of record in the specification;

claim 57 was rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita, Figdor, LaGrone, Haas, Charan and in further view of Matthiesen (WO 03/010188, hereinafter Matthiesen); and

claim 56 was rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita, Figdor, LaGrone, Haas, Charan, Matthiesen and in further view of Khwaja (US 5,547,674, hereinafter Khwaja).

These rejections are hereby traversed and reconsideration of the patentability of the pending claims is therefore requested in light of the following remarks.

Rejections under 35 U.S.C. §103

1. Claims 1-2, 6, 9, 15-16, 26-28. 37 and 81 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita and Figdor. Applicants insist that the proposed combination does not establish a prima facie case of obviousness.

According to the Office, the claims are obvious vis-à-vis the documents referred to since Arigita taught liposomes comprising a mannose targeting ligand and Figdor disclosed that fucose or mannose may be used to bind to C-type lectins on the surface of dendritic cells. According to the Examiner it would have been obvious to one of ordinary skill in the art to substitute a first targeting ligand as taught by Hartmann with the second targeting ligand, specifically fucose, capable of binding to C-type lectin-like carbohydrate recognition domains as taught by Figdor in view of Arigita with a reasonable expectation of success.

Applicants do not share this view of the Office, starting from the assumption that it was clear that there was an incentive for the skilled person to combine the teaching of all of these documents.

Initially, it should be noted that Hartmann does not disclose the targeting ligands of amended claims. Moreover, the interferon-producing cells of Hartmann are plasmacytoid dendritic cells (pDCs; see page 25, the paragraph below Table 2) which are not myeloid dendritic cells (mDCs). Finally, the approach of Hartmann is totally different from the approach of the presently claimed invention because Hartmann intends to elicit an HIV-specific immune response by inducing the release of interferon, while the present claims require the inactivation or eradication of the infectious agent by the active compound of the lipid complex itself.

Clearly, since the claims have been restricted to fucose, polyfucose or a derivative of polyfucose, Arigita (disclosing mannose as targeting ligand) is no longer relevant.

Thus, the question to be answered is whether the skilled person after having read Figdor could have chosen fucose as a targeting ligand. Applicants do not believe so because the approach of Figdor is totally different from the approach of the present application. Specifically, in Figdor a compound that binds to a C-type lectin, for example mannose, fucose, plant lectins etc. on the surface of a dendritic cell is used for the modulation of the immune response in a mammal. This is achieved by modulating the interaction between a dendritic cell and a T-cell. By use of the compounds that bind to a C-type lectin, the association of a C-type lectin receptor on a surface of dendritic cells with the ICAM receptors on the surface of T-cells could be reduced. However, it is interesting to note that Figdor does not show any experiments where this approach actually works. The claims

merely relate to antibodies that are capable of inhibiting binding between dendritic cells and T-cells. I t is even more important that none of the examples show experiments studying the effect of mannose, fucose, plant lectins etc.

Accordingly, the person skilled in the art would not have taken this document into account when trying to develop the claimed method being restricted to fucose as a targeting ligand since (a) the approach of Figdor is totally different from the approach of the present application and (b) Figdor does not show that his vague idea can actually be put into practice.

2. Claims 10 and 52 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita and Figdor and in further view of LaGrone. Again applicants insist that the proposed combination does not defeat the patentability of the presently claimed invention and certainly the addition of LaGrone does not overcome the shortcomings of the Hartmann, Arigita and Figdor combination.

According to the Office, LaGrone discloses a method of delivering an active agent to a reservoir cell, i.e. HIV-infected reservoir cells, comprising the administration of a plant lectin (col. 4, l. 8-24) encapsulated with a liposome (col. 10, l. 9). However, it is highly questionable to use a combination of at least four documents in order to deny an inventive step. The Office takes from Hartmann the general method, from Arigita and Figdor the targeting ligand and from LaGrone the particular active agent. Notably claim 10 depends from Claim 1, and as stated above, claim 1 is not defeated by the proposed combination of Hartmann, Arigita and Figdor. Thus, claim 10 and 52 are indeed patentable.

3. Claims 58-59 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, et al in view of Arigita, Figdor, LaGrone and in further view of Haas. As the number of references keeps increasing there is still no prima facie case of obviousness being established by the ever increasing number of references.

A detailed discussion of Haas and its relevance is not required since it is apparent that Haas neither discloses a particular lipid to a plant lectin ratio nor a particular size of the liposomes. The method of Haas is the modification of agents to be packaged having a low molecular weight in such a way that the membrane solubility or membrane permeability is improved. This approach is completely unrelated to the one claimed in the present application. Moreover, the Examiner may have

overlooked that claims 58 and 59 refer back to claim 52 which has already been restricted to fucose, polyfucose or polyfucose derivative as the targeting ligand.

4. Claims 50, 53, 56 and 57 were rejected under U.S.C. §103(a) as unpatentable over Hartmann, Arigita, Figdor, LaGrone, Haas and in further view of Charan and Matthiesen and Khwaja. Applicants insist that this multiplicity of references does not defeat the patentability of claim 50, 53, 56 and 57.

Firstly, applicants question the need for so many cited references in an attempt to establish a *prima facie* case of obviousness. Applicants submit that if the Office had a soundly based position on the issue of obviousness, it would not be necessary to rely on so many references. In this regard, the comments of the Board in *Ex Parte Blanc*, 13 USPQ2d 1383 (B.P.A.I. 1989) citing *Ball & Roller Bearing Co. v. F.C. Sanford Mfg. Co.*, 297 F. 163 (2d Cir. 1924) seem particularly pertinent. The Board stated that:

> "It seems necessary to apply to patent litigation from time to time the maxim that one cannot make omelettes of bad eggs--no matter how many are used. One good reference is better than 50 poor ones; and the 50 do not make the one any better."

Other Courts have agreed and have noted that the reliance on a large number of references is persuasive evidence of invention. See, e.g., *Handy v. American Flyer Mfg. Co.*, 6 USPQ 294 (S.D.N.Y. 1930) which stated that:

> "And the citation of many prior references, none showing a solution of the problem presented, is persuasive evidence of invention."

Applicants contend that the use by the Office of a multiplicity of references in an effort to show obviousness is in itself persuasive of the futility of attempting to establish a *prima facie* case of obviousness.

Applicants submit that even if all the extra references are added to that of Hartmann, Arigita, Figdor, LaGrone, Haas, the proposed combinations still do not teach or suggest each and every claimed limitation of the presently claimed invention.

In Sec. 14 to 16 of the Office Action the Office states that said claims lack an inventive step in light of a combination of several documents. The Office makes reference to Charan that teaches that MHL lectin has potent anti-HIV activity. With relation to claim 57, the Office refers to Matthiesen which discloses a means of preparing a pharmaceutical lectin formulation, wherein the active form

of the pharmaceutical lectin may be a dimer or a multimer. The Office refers to Khwaja for disclosing mistletoe extract comprising lectins as an anti-HIV pharmaceutical with some lectins being Ca^{2+}-depending sugar-binding proteins.

A detailed discussion of these additional documents does not seem to be required since an inventive step of these claims should be established due to the back reference to claim 52 being restricted to fucose, polyfucose or a polyfucose derivative.

Moreover, it has to be stressed that for the discussion of inventive step it is not relevant whether it was known that particular agents such as lectins inhibit HIV and/or other viruses. Instead the present invention relates to the use of lectins not as freely soluble agents, but as (a) encapsulated and (b) targeted compounds. This approach allows for the inhibition and destruction of intact and infectious viruses and their subunits when being present intracellularly in the particular cells – and exclusively in these cells – rather than to interfere with freely circulating viruses or their components. This novel and inventive approach claimed in the present application is by no means disclosed or suggested in the prior art.

In light of the above discussion, applicants expect that all rejections for obviousness be withdrawn.

Petition for Extension and Fees Payable

Applicants petition for a three month extension and the fee for such extension is being paid herewith by electronic transfer. Applicants have included herewith a RCE and the fee for such is being paid by electronic transfer. If any additional fee is found due, the U.S. Patent and Trademark Office is hereby authorized to charge any additional amount necessary to the entry of this amendment to Deposit Account No. 13-4365 of Moore & Van Allen PLLC.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Hill reconsider the patentability of pending claims in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Hill is requested to contact the undersigned attorney at (919) 286-8089 to resolve same.

Respectfully submitted,

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